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November 16, 2009

Carolyn M. Clancy, MD  
Director  
Agency for Healthcare Research and Quality  
Eisenberg Building  
540 Gaither Rd.  
Rockville, MD 20850

**RE: Technology Assessment: Report on the Evidence Regarding  
Off-Label Indications for Targeted Therapies Used in Cancer  
Treatment**

Dear Dr. Clancy:

On behalf of the Association of Community Cancer Centers (ACCC), we appreciate this opportunity to comment on the Agency for Healthcare Research and Quality's (AHRQ) draft Technology Assessment: Report on the Evidence Regarding Off-Label Indications for Targeted Therapies Used in Cancer Treatment (the "Draft Report").<sup>1</sup>

ACCC is a membership organization whose members include hospitals, physicians, nurses, social workers, and oncology team members who care for millions of patients and families fighting cancer. ACCC's more than 900 member institutions and organizations treat 60 percent of all U.S. cancer patients when combined with our physician membership.

ACCC is committed to ensuring that cancer patients have access to the entire continuum of quality cancer care, including access to the most appropriate cancer therapies. Cancer is a deadly disease, and patients often require treatment with the most innovative and cutting-

<sup>1</sup> Amy P. Abernethy et al. Report on the Evidence Regarding Off-Label Indications for Targeted Therapies Used in Cancer Treatment (August 26, 2009, released by AHRQ on October 7, 2009), available at: <http://www.ahrq.gov/clinic/ta/targthrps/targthrps.pdf> (hereinafter "Draft Report").

edge therapies to win their battles against it. Although some advances in cancer care are made by developing new drugs, many involve the discovery of new uses for drugs already approved for other indications by the Food and Drug Administration (FDA). This “off-label” use of cancer drugs is a common medical practice that is a critical component of many treatment regimens and is integral to the discovery of new cures.

The Centers for Medicare & Medicaid Services (CMS) requested this technology assessment of the efficacy and safety of selected targeted therapies when prescribed for off-label indications, with the secondary purpose of conducting a “horizon scan of early-stage trials (Phase I or prominent preclinical studies) of these agents.”<sup>2</sup> The Draft Report says, “CMS will consider this information as background to its further discussion of coverage for and policies regarding targeted therapies.”<sup>3</sup>

This technology assessment evaluates the strength of the evidence for 19 different drug/disease combinations using targeted therapies.<sup>4</sup> The reviewers searched four compendia to identify off-label indications for these drugs,<sup>5</sup> and conducted MEDLINE searches and searches of conference abstracts for evidence on the uses of these drugs for these indications.<sup>6</sup> The Draft Report makes several important observations that support the importance of the Medicare law and policy covering off-label uses of anti-cancer chemotherapeutic drugs supported by entries in certain compendia or by published research in certain journals.<sup>7</sup>

First, the Draft Report confirms “the pervasive sense among clinicians that the drug landscape in oncology is frequently changing.”<sup>8</sup> ACCC agrees that cancer care continually is evolving. In this challenging landscape, it is essential that Medicare and other payers maintain flexible coverage policies that provide access to anti-cancer drugs based on up-to-date clinical research. Medicare currently uses just such a flexible approach by covering uses supported in any of four compendia or by research published in any of 26 publications.

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<sup>2</sup> Id. at 12. “Targeted therapies” are defined as agents “designed not to kill cells but, more precisely, to attack growth factors, cell surface receptors, and intracellular proteins that mediate a malignancy’s ability to proliferate, grow, or evade cell death.” Examples of targeted therapies include small molecule inhibitors, monoclonal antibodies, and conjugated agents. Id. at 6.

<sup>3</sup> Id.

<sup>4</sup> Id. at 10.

<sup>5</sup> Id. at 13.

<sup>6</sup> Id. at 17-19.

<sup>7</sup> Social Security Act § 1861(t)(2); Medicare Benefit Policy Manual, ch. 15, § 50.4.5.

<sup>8</sup> Draft Report at 31.

Second, the Draft Report recognizes the important and challenging role the compendia play in clinical decision-making and coverage policy. The Draft Report notes that the compendia function as a “stepping stone” between drug development and research and FDA approval.<sup>9</sup> ACCC agrees with this observation. The compendia perform a critical service to patients, physicians, and policy-makers by collecting, analyzing, and disseminating the constantly-growing body of clinical research on cancer therapies. As the Draft Report recognizes, this is an enormous task, requiring the compendia to “continuously perform and updat[e] systematic reviews on the comprehensive list of FDA-approved drugs and biologics.”<sup>10</sup> Because this task is so substantial, it must be shared by a group of publications. Given the rapid changes in cancer care and supporting research, it is highly unlikely that any one publication could describe all of the medically accepted treatment options for every variety of cancer at any given point in time. Each publication applies a slightly different standard for inclusion and a different method of indicating whether a use is supported by clinical evidence and the weight of that evidence. For these reasons, ACCC supports Medicare’s recognition of multiple compendia, and we believe that any technology assessment of off-label uses of cancer therapies should examine all of the compendia currently used by Medicare.

Third, the Draft Report observes that a different standard may apply to evidence for cancer treatment than to treatments in other disciplines.<sup>11</sup> As the Draft Report notes, “in some diseases, despite limited and/or ambiguous data, the use of an off-label indication may be a reasonable clinical decision.”<sup>12</sup> In addition, “many cancers are potentially life-limiting diseases, for which there are few if any effective treatment options,” and “[o]ncologists and patients find themselves in a situation characterized by urgency, fear, and a desperate desire to take action in hopes of a response.”<sup>13</sup> ACCC agrees with these observations, and we ask AHRQ to include them in the final report. As CMS considers the evidence on off-label uses of FDA-approved therapies, it must recognize that patients and physicians must make treatment decisions under extremely difficult circumstances, and applying unduly strict standards to the clinical evidence will deny patients access to potentially life-saving care.

Finally, the Draft Report notes that “a different model of evidence generation and evaluation is warranted,” but asks, “is it possible?”<sup>14</sup> The Draft Report

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<sup>9</sup> Id. at 31.

<sup>10</sup> Id.

<sup>11</sup> Id. at 36.

<sup>12</sup> Id. at 34.

<sup>13</sup> Id.

<sup>14</sup> Id. at 36.

identifies “rapid learning healthcare” that “develops research insights as a natural byproduct of the care process” and comparative effectiveness research as “logical next area[s] of exploration in the effort to understand and improve upon the state of the evidence available to support medical care.”<sup>15</sup> ACCC strongly supports efforts to improve the quality of clinical evidence available to support treatment and policy decisions. We also acknowledge that treatment decisions must be made today with the information available now. Until any new research models are developed and implemented, CMS and other payers must continue to cover off-label treatments supported by the compendia or other published peer-reviewed research.

ACCC appreciates the opportunity to offer these comments. Please feel free to contact Matthew Farber at (301) 984-9496, if you have any questions or if ACCC can be of further assistance. Thank you for your attention to these very important matters.

Respectfully submitted,



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President

Association of Community Cancer Centers

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<sup>15</sup> Id. at 37.